REMARKS

Applicants thank the Examiner for the personal interview on March 20, 2003. A copy of the Interview Summary is included in Exhibit 1.

Applicants have amended claims 1, 2, 14, 22 and 23 to recite "selectable marker." Support for this amendment can be found throughout the specification. Applicants have also amended claims 1 and 14 to incorporate the subject matter of claim 7 as originally filed. Applicants have amended claim 2 to recite "in 6 x SSC under 55 °C." Support for this amendment can be found, for example, on page 27, line 17 of the specification. Applicants have amended claim 9 to incorporate the subject matter in claim 1 as originally filed and to delete the phrase "optionally comprising." Applicants have amended claim 10 to incorporate the subject matter of claim 1 as originally filed. Applicants have amended claims 11, 12 and 24 to depend from claim 36. Applicants have amended claim 19 to depend from amended claim 14 and to improve its form. Applicants have amended claims 29 and 30 to depend from claim 27 instead of claim 16. The above amendments are listed in Appendix 1.

Applicants have added claims 33-38. Support for the addition of claim 33 can be found, for example, in claims 1 and 7 as originally filed. Support for the addition of claims 34 and 35 can be found, for example, in claims 1, 7-8

and 13 as originally filed and on page 17, lines 23-31 of the specification. Support for the addition of claim 36 can be found, for example, in claims 1, 7 and 10 as originally filed. Support for the addition of claims 37 and 38 can be found, for example, on page 17, lines 16-31 of the specification.

Applicants have cancelled claims 6, 7 and 20 without prejudice. Applicants expressly reserve the right to pursue canceled or deleted subject matter in subsequent applications claiming benefit herefrom.

None of the amendments add new matter. Their entry is requested.

Information Disclosure Statement

The Examiner contends that Applicant's Form PTO-1449, filed August 29, 2002, was not available to the Examiner at the time of the November 20, 2002 Office Action. The Examiner requests applicants to submit a copy of the submitted form 1449.

Applicants submit herewith a copy of the submitted form 1449 in Exhibit 2.

§ 35 U.S.C. 112 First Paragraph Rejections

The Examiner has rejected claims 1-5, 8-9, 13 and 15-18, and newly added claims 21 and 24-32 under 35 U.S.C. 112, first paragraph, as containing subject matter which was

not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Examiner has also rejected claims 1-5, 8-13 and 15-20 and newly added claims 21-32 under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for other recombinant DNA molecules comprising other DNA sequences, or for products comprising said other recombinant DNA molecules, or for processes using said other recombinant DNA molecules. The Examiner contends that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants submit that these rejections have been withdrawn in the March 20, 2003 interview due to the representation of a number of 2-DOG-6-P phosphatase sequences available from the art (See Interview Summary).

§ 35 U.S.C. 112 Second Paragraph Rejections

In the Examiner's view, claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of hybridizes "under stringent conditions." The Examiner contends it is unclear under what stringency

conditions would yield the DNA sequences, as those skilled in the art define stringent conditions differently.

Applicants have amended claim 2 to replace "under stringent conditions" with a specific condition as suggested by the Examiner at the March 20, 2003 interview, thereby overcoming the rejection.

The Examiner contends that claim 19 is incomplete for omitting essential steps. The Examiner contends that the claimed method does not result in the production of a transgenic plant, plant cell tissue or combination thereof as set forth in the preamble.

Applicants have amended claim 19 to delete the phrases "a transgenic plant", "tissue, or a combination thereof" from the preamble, thereby overcoming the rejection.

§ 35 U.S.C. 103 Rejections

The Examiner has rejected claims 1-5, 8-13 and 15-20 and newly added claims 21-32 under 35 U.S.C. 103(a) as being unpatentable over Randez-Gil et al. (1995, Yeast, Vol. 11, pages 1233-1240) in view of Herrera-Estrella et al. (1983, The EMBO Journal, Vol. 2, pages 987-995), and in further view of Zemek et al. I (1975, Z. Pflanzenphysiol. Bd., Vol. 76, pages 114-119) and Zemek et al. II (1976, Z. Pflanzenphysiol. Bd., Vol. 77, pages 95-98).

Specifically, the Examiner contends that the success of Randez-Gil et al. in using a DNA sequence of SEQ

ID NO:1 encoding 2-deoxyglucose-6-phosphate phosphatase of SEQ ID NO:2 as a selectable marker in yeast cell culture, and the success of Herrera-Estrella et al. in using recombinant DNA molecules encoding other microbial enzymes as selectable markers in plant cell culture, would motivate one skilled in the art to use a DNA sequence of SEQ ID NO:1 encoding 2-deoxyglucose-6-phosphate phosphatase of SEQ ID NO:2 as a selectable marker in plant cell culture, especially given the teachings of Zemek et al. that 2-deoxyglucose inhibits the growth in plant cell cultures.

Applicants submit that in the March 20, 2003 interview, the Examiner withdrew the rejections for the method claims since there was unpredictability of using the 2-DOG-6-P phosphatase system in plants (See Interview Summary). Therefore, the method or process claims and added claims 36 and 37 are also not obvious in view of Randez-Gil et al., Herrera-Estrella et al. and Zemek et al. I and II.

The 2-DOG-6-P phosphatase system involves the 2-DOG-6-P phosphatase as a selection marker and the 2-DOG as a selection medium. As the actual function or substrate of the 2-DOG-6-P phosphatase in yeast is not known, it is unpredictable whether the phosphatase may modify other substrates in plants and interfere with the metabolism of plants. See page 1239, lines 44-45 of Randez-Gil et al. In addition, the presence of 2-DOG, a non-metabolizable analogue of glucose in the medium may interfere with the glucose

uptake and metabolism in plants. See page 118, lines 13-16 of Zemek I.

Applicants submit that the unpredictability of using the 2-DOG-6-P phosphatase system in plants also applies to the product claims. Further, one skilled in the art would not have been motivated to combine Randez-Gil, Herrera-Estrella, Zemek I and II and generate the claimed invention. Nowhere in Randez-Gil is there a teaching or suggestion to introduce the 2-DOG-6-P phosphatase gene into plants.

Herrera-Estrella only refers to processes and products involving the transformation and selection of plant cells using recombinant DNA molecules encoding *aminoglycoside phosphotransferase or methotrexate-insensitive dihydrofolate reductase*. It does not suggest using the recombinant DNA molecule comprising a DNA sequence encoding *2-deoxyglucose-6-phosphate phosphatase* to transform and select plant cells. In addition, the selection markers used in Herrera-Estrella are not similar enzymes to 2-DOG-6-P phosphatase, which detoxifies a metabolic intermediate product, 2-deoxyglucose-6-phosphate, which is derived from the selection agent 2-deoxyglucose (2-DOG). Aminoglycoside phosphotransferase phosphorylates and thereby inactivates the selection agent antibiotic. See page 992, left column first paragraph of Herrera-Estrella. Methotrexate-insensitive

dihydrofolate reductase is resistant to the selection agent methotrexate.

Furthermore, none of Zemek I and II mentions the 2-deoxyglucose-6-phosphate phosphatase gene. Zemek I and II merely teaches that 2-DOG inhibits growth in plants. As the mechanism for the inhibition of plant growth can be due to competitive inhibition of glucose metabolism by 2-DOG, Zemek I or II does not teach or suggest that introduction of the 2-DOG-6-P phosphatase in plants would cure the growth inhibition of plants cultured in 2-DOG, and thus, provide a selection system in plants. See page 118, last paragraph of Zemek I and page 98, last paragraph of Zemek II.

None of the above references teach or suggest using a 2-DOG-6-P phosphatase as a selection marker in plants. In coming to the conclusion that the claimed invention would have been *prima facie* obvious as a whole to one ordinary skilled in the art at the time the invention was made, the Examiner is clearly engaging in hindsight reconstruction.

In view of the lack of suggestion to combine the references and the unpredictability of the 2-DOG-6-P phosphatase system in plants, one skilled in the art would not have been motivated to combine Randez-Gil, Herrera-Estrella, Zemek I and II and generate the claimed invention with reasonable expectation of success.

Applicants have amended claims 1 and 14 to recite "a selectable marker" and a further DNA sequence. As

mentioned above, in view of the unpredictability of the interference of the 2-DOG-6-P phosphatase on plant metabolism, there is no motivation for one skilled in the art to combine the regulatory sequence of a promotor active in plants, the DNA sequence encoding a 2-DOG-6-P phosphatase sequence and a further DNA sequence in a recombinant molecule, host cell or plant cell, wherein the phosphatase sequence functions as a selectable marker for the further DNA sequence.

Applicants have also amended claim 9 to include the 2-DOG or a non-metabolizable analogue of glucose in the kit. As mentioned above, in view of the unpredictability of the 2-DOG-6-P phosphatase system in plants, it is not obvious for one skilled in the art to produce a kit with a regulatory sequence of a promotor active in plants, a DNA sequence encoding a 2-DOG-6-P phosphatase sequence, and 2-DOG or a non-metabolizable analogue of glucose. Therefore, claims 1-5, 8-9, 13-35 and 38 are not obvious in view of Randez-Gil et al., Herrera-Estrella et al. and Zemek et al. I and II.

CONCLUSION

Applicants respectfully request that the Examiner reconsider and withdraw all outstanding rejections, enter the proposed amendments and additions, and pass the claims to allowance. If the Examiner believes that a telephone conference would expedite allowance of this application, she is invited to telephone the undersigned at any time.

Respectfully submitted,

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Appendix 1

1. (Twice Amended) A recombinant DNA molecule comprising a regulatory sequence of a promotor active in plants, a selectable marker DNA sequence encoding a 2-deoxyglucose-6-phosphate (2-DOG-6-P) phosphatase operably linked thereto and a further DNA sequence encoding a peptide, protein, antisense or sense RNA, viral RNA or a ribozyme.

2. (Twice Amended) The recombinant DNA molecule of claim 1, wherein the selectable marker DNA sequence is selected from the group consisting of:

(a) a DNA sequence which encodes the amino acid sequence of SEQ ID NO: 2;

(b) a DNA sequence of SEQ ID NO: 1;

(c) a DNA sequence which hybridizes [under stringent conditions] in 6 x SSC under 55 °C to a complementary strand of the DNA sequence of (a) or (b);

(d) a DNA sequence which is degenerate to the DNA sequence of (b) or (c); and

(e) a DNA sequence encoding a polypeptide amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO: 2 and having 2-DOG-6-P phosphatase activity.

9. (Twice Amended) A kit comprising [the recombinant DNA molecule of claim 1 or 2, or a vector comprising said recombinant DNA molecule and optionally comprising] a DNA sequence comprising a regulatory sequence of a promotor active in plants and a sequence encoding a 2-deoxyglucose-6-phosphate (2-DOG-6-P) phosphatase operably linked thereto or a vector comprising said DNA sequence, and 2-deoxyglucose or a non-metabolizable analogue of glucose.

10. (Twice Amended) A process for selecting a transformed plant cell, comprising the following steps:

(a) obtaining plant cells;

(b) introducing [the recombinant DNA molecule of claim 1 or 2,] a DNA sequence comprising a regulatory sequence of a promotor active in plants and a sequence encoding a 2-deoxyglucose-6-phosphate (2-DOG-6-P) phosphatase operably linked thereto, or a vector comprising said [recombinant DNA molecule] DNA sequence into said plant cells; and

(c) selecting the successfully transformed plant cell on 2-deoxyglucose-containing media or on media containing a non-metabolizable analogue of glucose.

11. (Twice Amended) The process of claim 10 or 36, wherein the vector is transferred to plant cells via Agrobacterium tumefaciens.

12. (Amended) The process of claim 10 or 36, wherein the recombinant DNA molecule or vector is transferred to plant cells by particle bombardment.

14. (Twice Amended) [The] A transgenic plant cell [of claim 13] comprising a DNA sequence comprising a regulatory sequence of a promotor active in plants and a selectable marker sequence encoding a 2-deoxyglucose-6-phosphate (2-DOG-6-P) phosphatase operably linked thereto, and at least one further [foreign gene] DNA sequence encoding a peptide, protein, antisense or sense RNA, viral RNA or a ribozyme.

19. (Twice Amended) A method of producing [a transgenic plant,] [a] the plant cell of claim 14 [, tissue, or a combination thereof from the recombinant DNA molecule of

claim 1 or 2, a vector comprising said recombinant DNA molecule] comprising:

a) obtaining a plant cell; and

b) introducing the DNA sequence and the further DNA sequence [the recombinant DNA molecule or vector] into the plant cell.

22. (Amended) The recombinant DNA molecule of claim 1, wherein the selectable marker DNA sequence encodes the amino acid sequence of SEQ ID NO: 2.

23. (Amended) The recombinant DNA molecule of claim 1, wherein the selectable marker DNA sequence is SEQ ID NO: 1.

24. (Amended) A transgenic plant cell produced according to the process of claim 10 or 36.

29. (Amended) The transgenic plant of claim [16] 27, wherein the plant is a monocotyledonous or dicotyledonous plant.

30. (Amended) The transgenic plant of claim [16] 27, wherein the plant is selected from the group consisting of wheat, barley, rice, rape, pea, maize, sugar beet, sugar cane and potato.